

What is claimed:

1. A method of killing a tumor cell comprising contacting the cell with at least one small inhibitory RNA (siRNA) specific for a DNA repair protein and at least one DNA-damaging agent.
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2. The method of claim 1, wherein the DNA repair protein is selected from the group consisting of ATM, ATR, and DNA-PK_{cs}.
- 10 3. The method of any one of claims 1 or 2, wherein the siRNA is encoded by a nucleic acid sequence selected from the group consisting of SEQ ID NO:1, 2, 4, 5, 7, 8, 10, 11, 13, 14, 16, 17, 19, 20, 22, 23, 25, 26, 28, 29, 30, 31, 32, 33, 34, 35, or 36.
- 15 4. The method of any one of claims 1-3, wherein the DNA-damaging agent is radiation.
5. The method of any one of claims 1-3, wherein the DNA-damaging agent is a chemotherapeutic agent.
- 20 6. The method of claim 5, wherein the chemotherapeutic agent is an alkylating agent.
- 25 7. The method of claim 6, wherein the alkylating agent is selected from the group consisting of a nitrogen mustard, an aziridine, an alkyl sulfonate, a nitrosurea, a platinum complex, and a nonclassic alkylator.
- 30 8. The method of claim 7, wherein the nitrogen mustard is selected from the group consisting of chlorambucil, cyclophosphamide, estramustine, ifosfamide, mechlorethamine, and melphalan.
9. The method of claim 7, wherein the aziridine is thiotepa.
10. The method of claim 7, wherein the alkyl sulfonate is busulfan.

11. The method of claim 7, wherein the nitrosurea is selected from the group consisting of carmustine, lomustine, and streptozocin.

12. The method of claim 7, wherein the platinum complex is selected from the
5 group consisting of carboplatin and cisplatin.

13. The method of claim 7, wherein the nonclassic alkylator is selected from the group consisting of altretamine, dacarbazine, procarbazine, and temozolamide.

10 14. The method of claim 4, further comprising contacting the cell with at least one chemotherapeutic agent.

15. The method of any one of claims 5-14, further comprising contacting the cell with at least a second chemotherapeutic agent.

15 16. The method of any one of claims 1-15, wherein the tumor cell is derived from a cell or tissue type selected from the group consisting of prostate, colon, breast, lung, brain, skin, ovary, pancreas, liver, stomach, bladder, bone, testicle, uterus, adipose tissue, throat, kidney, tongue, pituitary gland, thyroid, nerve, lymphoid tissue, eye, and cervix.

20 17. The method of any one of claims 1-16, wherein the tumor cell is resistant to killing by contacting with the DNA damaging agent alone.

25 18. The method of any one of claims 1-17, wherein the siRNA is expressed from a vector.

19. The method of claim 18, wherein the vector is a plasmid.

20. The method of claim 18, wherein the vector is an adenoviral vector.

30 21. The method of any one of claims 1-20, wherein expression of the siRNA is controlled by a modified adenoviral promoter.

22. The method of claim 21, wherein the modified adenoviral promoter comprises, in sequence, an adenoviral VA1 A-Box, at least one restriction enzyme recognition site, at least one adenoviral VA1 termination sequence, and at least one adenoviral VA1 B-box.

5 23. A method of treating a subject having cancer comprising administering to the subject a therapeutically effective amount of at least one small inhibitory RNA (siRNA) specific for a DNA repair protein and a therapeutically effective amount of at least one DNA-damaging agent.

10 24. The method of claim 23, wherein the DNA repair protein is selected from the group consisting of ATM, ATR, and DNA-PK_{cs}.

15 25. The method of any one of claims 23-24, wherein the siRNA is encoded by a nucleic acid sequence selected from the group consisting of SEQ ID NO:1, 2, 4, 5, 7, 8, 10, 11, 13, 14, 16, 17, 19, 20, 22, 23, 25, 26, 28, 29, 30, 31, 32, 33, 34, 35, or 36.

26. The method of any one of claims 23-25, wherein the DNA-damaging agent is radiation.

20 27. The method of any one of claims 23-256, wherein the DNA-damaging agent is a chemotherapeutic agent.

28. The method of claim 27, wherein the chemotherapeutic agent is an alkylating agent.

25 29. The method of claim 28, wherein the alkylating agent is selected from the group consisting of a nitrogen mustard, an aziridine, an alkyl sulfonate, a nitrosurea, a platinum complex, and a nonclassic alkylator.

30 30. The method of claim 29, wherein the nitrogen mustard is selected from the group consisting of chlorambucil, cyclophosphamide, estramustine, ifosfamide, mechlorethamine, and melphalan.

31. The method of claim 29, wherein the aziridine is thiotepa.

32. The method of claim 29, wherein the alkyl sulfonate is busulfan.
33. The method of claim 29, wherein the nitrosurea is selected from the group consisting of carmustine, lomustine, and streptozocin.
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34. The method of claim 29, wherein the platinum complex is selected from the group consisting of carboplatin and cisplatin.
- 10 35. The method of claim 29, wherein the nonclassic alkylator is selected from the group consisting of altretamine, dacarbazine, procarbazine, and temozolamide.
36. The method of claim 26, further administering to the subject a therapeutically effective amount of at least one chemotherapeutic agent.
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37. The method of any one of claims 27-36, further administering to the subject a therapeutically effective amount of at least a second chemotherapeutic agent.
- 20 38. The method of any one of claims 23-37, wherein the cancer is derived from a cell or tissue type selected from the group consisting of prostate, colon, breast, lung, brain, skin, ovary, pancreas, liver, stomach, bladder, bone, testicle, uterus, adipose tissue, throat, kidney, tongue, pituitary gland, thyroid, nerve, lymphoid tissue, eye, and cervix.
- 25 39. The method of any one of claims 23-37, wherein the cancer is resistant to treatment by administration of the DNA damaging agent alone.
40. The method of any one of claims 23-39, wherein the siRNA is expressed from a vector.
- 30 41. The method of claim 40, wherein the vector is a plasmid.
42. The method of claim 40, wherein the vector is an adenoviral vector.

43. The method of any one of claims 23-42, wherein expression of the siRNA is controlled by a modified adenoviral promoter.

44. The method of claim 43, wherein the modified adenoviral promoter comprises, 5 in sequence, an adenoviral VA1 A-Box, at least one restriction enzyme recognition site, at least one adenoviral VA1 termination sequence, and at least one adenoviral VA1 B-box.

45. The method of any one of claims 23-44, wherein the siRNA is administered to the subject systemically.

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46. The method of any one of claims 23-44, wherein the siRNA is administered to the subject locally at the site of a tumor.

47. The method of any one of claims 23-46, wherein the siRNA is administered 15 prior to administration of the DNA-damaging agent.

48. The method of any one of claims 23-46, wherein the siRNA is administered at the same time as the DNA-damaging agent.

20 49. The method of any one of claims 23-46, wherein the DNA-damaging agent is administered prior to the siRNA.

50. An isolated nucleic acid molecule comprising a modified adenoviral promoter, 25 wherein the modified adenoviral promoter comprises, in sequence, an adenoviral VA1 A-Box, at least one restriction enzyme recognition site, at least one adenoviral VA1 termination sequence, and at least one adenoviral VA1 B-box.

51. A isolated nucleic acid molecule comprising a nucleic acid sequence selected 30 from the group consisting of SEQ ID NO:1, 2, 4, 5, 7, 8, 10, 11, 13, 14, 16, 17, 19, 20, 22, 23, 25, 26, 28, 29, 30, 31, 32, 33, 34, 35, or 36.